

From the INTERNATIONAL BUREAU

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NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis.1(c))

To:

PEAUCELLE, Chantal
Cabinet Armentaud et
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FRANCE

15 SEP. 2006**RECU**Date of mailing (*day/month/year*)

08 September 2006 (08.09.2006)

Applicant's or agent's file reference

CP 61262

IMPORTANT NOTICE

International application No.

PCT/EP2005/002577

International filing date (*day/month/year*)

24 February 2005 (24.02.2005)

Priority date (*day/month/year*)

26 February 2004 (26.02.2004)

Applicant

THERAPTOSIS S.A. et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference CP 61262	FOR FURTHER ACTION	See item 4 below
International application No. PCT/EP2005/002577	International filing date (<i>day/month/year</i>) 24 February 2005 (24.02.2005)	Priority date (<i>day/month/year</i>) 26 February 2004 (26.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THERAPTOSIS S.A.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.
3. This report contains indications relating to the following items:

<input checked="" type="checkbox"/> Box No. I	Basis of the report
<input type="checkbox"/> Box No. II	Priority
<input type="checkbox"/> Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/> Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/> Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/> Box No. VI	Certain documents cited
<input type="checkbox"/> Box No. VII	Certain defects in the international application
<input type="checkbox"/> Box No. VIII	Certain observations on the international application
4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis*.2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 30 August 2006 (30.08.2006)
Facsimile No. +41 22 338 82 70	Authorized officer <div style="text-align: right;">Yolaine Cussac</div>
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 28 JUN 2005

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To:

see form PCT/ISA/220

9/9

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/002577

International filing date (day/month/year)
24.02.2005

Priority date (day/month/year)
26.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07K14/80, C12Q1/26

Applicant
THERAPTOSIS S.A.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/002577

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/002577

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-20
	No: Claims	
Inventive step (IS)	Yes: Claims	1-20
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-20
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Basis for the assessment of novelty, inventive step and industrial applicability

1.1 Reference is made to the following document/s/:

- D1: "A NEW QUANTITATIVE ASSAY FOR CYTOCHROME C RELEASE IN APOPTOTIC CELLS" CELL DEATH AND DIFFERENTIATION, EDWARD ARNOLD, OXFORD, GB, vol. 10, no. 7, July 2003 (2003-07), pages 853-855, XP001206771 ISSN: 1350-9047
- D2: LU W ET AL: "Use of Prussian blue/conducting polymer modified electrodes for the detection of cytochrome C" ELECTROANALYSIS, vol. 10, no. 7, June 1998 (1998-06), pages 472-476, XP009048727 ISSN: 1040-0397
- D3: LU WEN ET AL: "Detection of cytochrome c using a conducting polymer mediator containing electrode" ELECTROANALYSIS, vol. 8, no. 3, 1996, pages 248-252, XP009048726 ISSN: 1040-0397
- D4: SMITH L: "Spectrophotometric assay of cytochrome c oxidase." METHODS OF BIOCHEMICAL ANALYSIS. 1955, vol. 2, 1955, pages 427-434, XP009048732 ISSN: 0076-6941
- D5: CATINO J J ET AL: "Microtiter assay useful for screening of cell-differentiation agents." JOURNAL OF THE NATIONAL CANCER INSTITUTE. 17 AUG 1988, vol. 80, no. 12, 17 August 1988 (1988-08-17), pages 962-966, XP009048730 ISSN: 0027-8874
- D6: PICKLO M J ET AL: "High-pressure liquid chromatography quantitation of cytochrome c using 393 nm detection." ANALYTICAL BIOCHEMISTRY. 15 DEC 1999, vol. 276, no. 2, 15 December 1999 (1999-12-15), pages 166-170, XP002332121 ISSN: 0003-2697
- D7: ISHIHARA T ET AL: "Detection of cytochrome C by means of surface plasmon resonance sensor" SENSORS AND ACTUATORS B, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 91, no. 1-3, 1 June 2003 (2003-06-01), pages 262-265, XP004424428 ISSN: 0925-4005

D8: CHRZANOWSKA-LIGHTOWLERS Z M ET AL: "A microtiter plate assay for cytochrome c oxidase in permeabilized whole cells." ANALYTICAL BIOCHEMISTRY. OCT 1993, vol. 214, no. 1, October 1993 (1993-10), pages 45-49, XP002332122 ISSN: 0003-2697

2. Novelty

- 2.1 Claim 1 appears to be novel over the available prior art (Art 33(2) PCT). Dependent claims 2-6 are thus also novel (Art 33(2) PCT).
- 2.2 Claim 7 and claims 8-20 dependent thereon appear to be novel over the available prior art (Art 33(2) PCT).

3. Inventive step

- 3.1 The prior art discloses a number of different methods to detect cytochrome C. D1 discloses Western blotting, immunocytochemistry and the use of GFP-tagged cytochrome C for intracellular detection. Both D2 and D3 describe a method whereby cytochrome C is detected taking advantage of its electrochemical properties and a suitable electrode. D4 discloses an assay whereby cytochrome C oxidase is used and in D5 the reduction of cytochrome C by a cell lysate is measured spectrometrically. D6 proposes a chromatographic method and D7 a method based on plasmon resonance. D8, finally, discloses a coupled assay for the measurement of cytochrome C oxidase whereby cytochrome C cycles between its oxidised and reduced state.

The prior art, however, appears not to contain any indication to a method as suggested in claim 1.

Thus claim 1 provides an inventive solution to the technical problem of providing a further method for cytochrome C detection (Art 33(3) PCT). Dependent claims 2-6 are thus also inventive.

Claim 7 referring to a kit specially adapted to the method of claim 1, thus also appears to be inventive (Art 33(3) PCT). Dependent claims 8-20 are thus also

inventive (Art 33(3) PCT).

4. Industrial applicability

- 4.1 The subject-matter disclosed in the claims 1-20 of the present application appears to be industrially applicable (Art 33(4) PCT).

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